REMARKS

Initially, Applicants note that on December 13, 2002, Applicants submitted (and the USPTO received) in this application a new power of attorney document (providing the undersigned power to prosecute this application) and a request for a change of correspondence address. In that document, it was requested that all future correspondence be sent to the undersigned attorney at Genentech, Inc., 1 DNA Way, MS49, South San Francisco, CA 94080. Applicants note that the current Office Action, however, was sent to a different mailing address. Applicants respectfully request that all future correspondence for this application be sent to the address requested in the document filed with the PTO on December 13, 2002. A copy of this power of attorney and change of correspondence document (as well as a copy of the return receipt postcard evidencing safe receipt by the USPTO) is enclosed herewith.

Claims 1-13 were pending for prosecution in this application. Applicants have herein canceled Claims 1-13 and have added new Claims 14-16, wherein support for the newly added claims can be found in the specification at least in the claims as originally filed.

Applicants have amended the specification so as to properly recognize certain trademarks presented therein, as suggested by the Examiner.

The Rejections under 35 U.S.C. § 101

Claims 1-13 stand rejected under 35 U.S.C. § 101 as allegedly not being supported by either a specific and substantial asserted utility or a well-established utility. The cancellation of these claims also renders this rejection moot, however, because new Claims 14-16 encompass similar (as well as overlapping subject matter), Applicants will respond as if this rejection applies to the newly added claims herein. Applicants respectfully traverse the rejection.

Initially, Applicants respectfully direct the Examiner to Example 18 starting on page 140 of the current specification which provides an analysis that is useful for identifying molecules that are differentially expressed in human tumor samples as compared to the corresponding normal tissue.

With more specific regard to the presently claimed subject matter, the Examiner is respectfully directed to the specific data in Example 18 for DNA59610-1556 which demonstrates that that specific molecule is detectably overexpressed in human esophageal tumor as compared to its normal tissue counterpart (i.e., normal human esophageal tissue) and is also detectably overexpressed in human lung tumor as compared to its normal tissue counterpart (i.e., normal human lung tissue). This data is specific for DNA59610-1556 (i.e., SEQ ID NOS:59 and 60). Clearly, therefore, these data support the conclusion recited in Example 18 that the "identification of the differential expression of the PRO polypeptide-encoding nucleic acid in one or more tumor tissues as compared to one or more normal tissues of the same tissue type renders the molecule useful diagnostically for the determination of the presence or absence of tumor in a subject suspected of possessing a tumor". In other words, the presently claimed polypeptides are useful as diagnostic targets for the determination of esophageal or lung tumor in human tissue samples of previously unknown morphology. Applicants submit, therefore, that the data presented in Example 18 clearly demonstrates a specific, substantial and credible utility for the presently claimed invention.

Moreover, as clearly disclosed in the present specification, the polypeptides recited in the present claims are useful as immunogens for the preparation of antibodies that bind to the polypeptide shown herein as SEQ ID NO:60. Techniques for producing monoclonal antibodies are well known and routinely used in the art, wherein such antibodies are useful for the quantitative determination of the expression level of DNA59610-1556 in human tissue samples. As the data presented in the present specification shows that this molecule is detectably overexpressed in human esophageal and lung tumors as compared to the corresponding normal tissue type, such antibodies are useful as diagnostic probes for making these quantitative determinations. As such, the presently claimed polypeptides also find specific, substantial and credible use for generating antibody probes that are diagnostically useful.

In light of the above, Applicants respectfully request reconsideration and withdrawal of the outstanding rejection.

The Rejection under 35 U.S.C. § 112, Second Paragraph

Claims 1-6 and 10 stand rejected under 35 U.S.C. § 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Cancellation of these claims hereby renders this rejection moot.

The Rejection under 35 U.S.C. § 112, First Paragraph

A. The "Enablement" Rejection

Claims 1-13 stand rejected under 35 U.S.C. § 112, first paragraph, as the claimed invention is allegedly not supported by a specific or substantial utility. Moreover, Claims 1-5 and 12-13 stand rejected under 35 U.S.C. § 112, first paragraph, as "the specification, were it enabled for an isolated polypeptide comprising SEQ ID NO:60 or at least the mature form of SEQ ID NO:60, would still not reasonably provide enablement for polypeptides having at least 80%, 85%, 90%, 95% or 99% amino acid sequence identity to the polypeptide of SEQ ID NO:60." Applicants respectfully traverse the rejection.

Initially, Applicants note that Claims 1-13 have been herein canceled and replaced with new Claims 14-16. New Claims 14-16 no longer make reference to polypeptides that are at least 80%, 85%, 90%, 95% or 99% identical to SEQ ID NO:60. As such, the rejection such as it is directed to such claim language is no longer applicable.

New Claims 14-16 recite the following isolated polypeptides: (a) the polypeptide of SEQ ID NO:60, (b) the mature form of the polypeptide of SEQ ID NO:60 (i.e., amino acids 29-282 of SEQ ID NO:60), (c) a soluble extracellular domain form of the polypeptide of SEQ ID NO:60 (i.e., amino acids 1-257 of SEQ ID NO:60), (d) a polypeptide comprising the amino acid sequence encoded by the full-length coding sequence of SEQ ID NO:59 and (e) a polypeptide comprising the amino acid sequence encoded by the full-length coding sequence of the cDNA vector deposited with the ATCC under ATCC accession no. 209990.

With regard to enablement for the claimed isolated polypeptides, the specification provides the complete nucleotide sequence of DNA59610-1556 (SEQ ID NO:59) and the location of the relevant start and stop codons (see Figure 59). The specification also provides the complete amino acid sequence encoded thereby and the location of the signal peptide found in that full-length polypeptide (see Figure 60), thereby teaching the sequence of the mature polypeptide (i.e., amino acids 29-282 of SEQ ID NO:60). Furthermore, the specification also provides the location of the transmembrane domain found in that full-length polypeptide (see Figure 60), thereby teaching the sequence of the N-terminal soluble extracellular domain fragment of the full-length polypeptide (i.e., amino acids 1-257 of SEQ ID NO:60). Moreover, as described in the specification, a vector comprising the full-length cDNA sequence disclosed herein as SEQ ID NO:59 has been deposited under the terms of the Budapest Treaty with the ATCC as ATCC accession number 209990. As such, Applicants respectfully submit that it certainly would not require undue experimentation on the part of one of ordinary skill in the art to "make" any of the above described isolated polypeptides as recited in the present claims.

With regard to how to "use" any of the above described isolated polypeptides, as described above, Applicants have demonstrated that DNA59610-1556 is detectably overexpressed in human esophageal and lung tumors as compared to their normal, non-cancerous respective counterpart tissues. Therefore, quantitative determination of the level of expression of DNA59610-1556 in a human tissue sample of unknown pathology is clearly useful for the diagnostic determination of both esophageal and lung cancer in humans. This is clearly described and set forth in the present specification. Techniques for exploiting polypeptide targets for the quantitative measurement of polypeptide expression in a human tissue sample (including, for example, immunohistochemistry and Western blotting) are well known and routinely used in the art and are described in detail in the present specification. Moreover, techniques for using an isolated polypeptide as an immunogen against which an antibody may be generated are also well known and routinely used in the art, wherein the antibody would find use for the quantitative determination of the level of expression of

the polypeptide encoded by the nucleic acid of SEQ ID NO:59. As such, Applicants respectfully submit that the present specification, taken with what is well known and routinely employed in the art, clearly teaches how to make and use the claimed invention without undue experimentation. It is believed, therefore, that the outstanding rejection under 35 U.S.C. § 112, first paragraph, for lack of enablement is improper and should be withdrawn.

B. The "Written Description" Rejection

Claims 1-5 and 12-13 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly "containing subject matter which was not described in the specification in such as way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention". In this regard, Applicants have herein canceled the rejected claims, thereby obviating this rejection. It is believed that new Claims 14-16 clearly comply with the written description requirement of 35 U.S.C. § 112, first paragraph.

The Rejections under 35 U.S.C. § 102(e)

Claims 1-12 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 6,468,546. Moreover, Claims 1-13 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by (a) Chen (U.S. Patent Application Publication 2002/0168762), (b) Ople et al. (U.S. Patent Application Publication 2002/0051990) and (c) Fox et al. (U.S. Patent Application Publication 2002/0165347). Applicants respectfully traverse the rejections.

Initially, Applicants first note that the present application was filed on May 2, 2002 and claims priority to at least PCT/US99/12252, filed on August 24, 2000. In the present Office Action, the Examiner asserts on the record that the presently claimed subject matter has an effective filing date of this PCT application, namely August 24, 2000 (see the present Office Action at page 2, first full paragraph).

Moreover, Applicants note that the herein cited Chen publication was filed on July 26, 2001 (i.e., after the August 24, 2000 effective priority date of the present application afforded by the Examiner). As such, the Chen reference can only be effective prior art under 35 U.S.C. § 102(e) to the present application if it is entitled to its claimed priority date (i.e., U.S. provisional application serial no. 60/220,991, filed on July 27, 2000). In other words, the Chen reference cannot be anticipating prior art to the present claimed invention unless the priority document claimed by the Chen published application has an anticipating disclosure to the presently claimed invention. As the provisional application to which the herein cited Chen publication claims priority is not available to Applicants and was not provided to the Applicants by the Examiner, it is not possible for Applicants to determine whether Chen is, or is not, entitled to a prior art date which is earlier than their July 26, 2001 filing date. As such, without the Examiner providing such prima facie evidence, Applicants must assume that the effective prior art date of the Chen publication is its filing date, namely July 26, 2001. In this case, therefore, the Chen publication is simply not effective prior art under 35 U.S.C. § 102(e) to the present application. The rejection with regard to the Chen reference, therefore, should be withdrawn.

Additionally, the same situation applies to the herein cited Ople et al. reference. Applicants note that the herein cited Ople et al. publication was filed on June 11, 2001 (i.e., after the August 24, 2000 effective priority date of the present application afforded by the Examiner). As such, the Ople et al. reference can only be effective prior art under 35 U.S.C. § 102(e) to the present application if it is entitled to its claimed priority date (i.e., U.S. provisional application serial no. 60/210,451, filed on June 9, 2000). In other words, the Ople et al. reference cannot be anticipating prior art to the present claimed invention unless the priority document claimed by the Ople et al. published application has an anticipating disclosure to the presently claimed invention. As the provisional application to which the herein cited Ople et al. publication claims priority is not available to Applicants and was not provided to the Applicants by the Examiner, it is not possible for Applicants to determine whether Ople et al. is, or is not, entitled to a prior art date which is earlier than their

June 11, 2001 filing date. As such, without the Examiner providing such prima facie evidence, Applicants must assume that the effective prior art date of the Ople et al. publication is its filing date, namely June 11, 2001. In this case, therefore, the Ople et al. publication is simply not effective prior art under 35 U.S.C. § 102(e) to the present application. The rejection with regard to the Ople et al. reference, therefore, should be withdrawn.

Finally, the same situation applies to the herein cited Fox et al. reference. Applicants note that the herein cited Fox et al. publication was filed on June 29, 2001 (i.e., after the August 24, 2000 effective priority date of the present application afforded by the Examiner). As such, the Fox et al. reference can only be effective prior art under 35 U.S.C. § 102(e) to the present application if it is entitled to its claimed priority date (i.e., U.S. provisional application serial no. 60/215,645, filed on June 30, 2000). In other words, the Fox et al. reference cannot be anticipating prior art to the present claimed invention unless the priority document claimed by the Fox et al. published application has an anticipating disclosure to the presently claimed invention. As the provisional application to which the herein cited Fox et al. publication claims priority is not available to Applicants and was not provided to the Applicants by the Examiner, it is not possible for Applicants to determine whether Fox et al. is, or is not, entitled to a prior art date which is earlier than their June 29, 2001 filing date. As such, without the Examiner providing such prima facie evidence, Applicants must assume that the effective prior art date of the Fox et al. publication is its filing date, namely June 29, 2001. In this case, therefore, the Fox et al. publication is simply not effective prior art under 35 U.S.C. § 102(e) to the present application. The rejection with regard to the Fox et al. reference, therefore, should be withdrawn.

With respect to the herein cited U.S. Patent No. 6,468,546 reference, the effective prior art date thereof is September 24, 1999 (a date which Applicants note is earlier than any of the priority dates claimed by the Chen, Ople et al. and Fox et al. published applications). As such, the effective 35 U.S.C. § 102(e) date of the U.S. Patent No. 6,468,546 reference is less than one year prior to the August 24, 2000 effective priority date of the present application.

In light of the above, Applicants enclose herewith a declaration under 37 C.F.R. § 1.131 signed by William I. Wood, Ph.D. (an inventor of the claimed invention) which serves to swear back of the herein references, and thereby remove them as references that can be relied upon in support of a rejection under 35 U.S.C. § 102(a). More specifically, Dr. Wood provides facts demonstrating that the present Applicants had conceived of and reduced to practice the polypeptides of the present invention before the effective prior art dates of the herein cited references. Relevant case law specifically makes clear that such a declaration under 37 C.F.R. § 1.131 is sufficient in this situation to remove the herein cited references as prior art which can be relied upon by the Examiner in support of a rejection under 35 U.S.C. § 102(e).

Relevant Case Law

In support of Applicants conclusion, the Examiner is first respectfully directed to *In re Stempel*, 113 USPQ 77 (CCPA 1957) where the patent applicant (Stempel) had claims directed to both (i) a particular genus of chemical compounds (the "generic" claim) and (ii) a single species of chemical compound that was encompassed within that genus (the "species" claim). In support of a rejection under 35 U.S.C. § 102, the examiner cited against the Stempel application a prior art reference that disclosed the exact chemical compound recited in Stempel's "species" claim. In response to the rejection, Stempel filed a declaration under 37 C.F.R. § 1.131 demonstrating that he had made that specific chemical compound prior to the effective date of the cited prior art reference. The lower court found the 131 declaration effective to "swear back" of the prior art reference for purposes of allowing a claim to the specific species. However, relying on the doctrine that prior disclosure of a species is sufficient to anticipate a later claim to a genus encompassing that species, the lower court ruled the 131 declaration ineffective for swearing behind the cited references for purposes of the "genus" claim.

On appeal, however, the CCPA reversed the decision of the lower court and found Stempel's 131 declaration effective for swearing behind the cited reference for purposes of both the "species" claim and the "genus" claim. Specifically, the CCPA stated in support of its decision:

> "We are convinced that under the law all the applicant can be required to show [in a declaration under 37 C.F.R. § 1.131] is priority with respect to **so much of the claimed invention as the reference happens to show**. When he has done this he has disposed of the reference." (*Id.* at 81; emphasis supplied).

Thus, the well established "Stempel Doctrine" stands for the clear proposition that a patent applicant can effectively swear back of and remove a cited prior art reference merely by showing that he or she made only that portion of the claimed invention that is disclosed in the prior art reference. In other words, a patent applicant need not demonstrate that he or she made his or her entire claimed invention in order to remove a cited prior art reference under 37 C.F.R. § 1.131.....to the contrary, he or she only need show prior possession of that portion of his or her claimed invention that is disclosed in the prior art reference; nothing more is required.

Secondly, the Examiner is next respectfully directed to *In re Moore*, 170 USPQ 260 (CCPA 1971), where the Stempel rule was applied to cases where a reference disclosed the claimed compound but no failed to disclose a sufficient utility for it. More specifically, the patent applicant (Moore) claimed a specific chemical compound called PFDC. In support of a rejection of the claim under 35 U.S.C. § 102, the examiner cited a reference which disclosed the claimed PFDC compound, but did not disclose a utility for that compound. Applicant Moore filed a declaration under 37 C.F.R. § 1.131 demonstrating that he had made the PFDC compound before the effective date of the cited prior art reference, even though he had not yet established a utility for that compound. The lower court found the 131 declaration ineffective to swear back of and remove the cited reference, reasoning that since Moore had not established a utility for the PFDC compound prior to the effective date of the cited prior art reference, he had not yet completed his "invention".

On appeal, however, the CCPA reversed the lower court decision and indicated that the 131 declaration filed by Moore was sufficient to remove the cited reference. The CCPA relied on the established "Stempel Doctrine" to support its decision, stating:

> "An applicant need **not** be required to show [in a declaration under 37 C.F.R. § 1.131] any more acts with regard to the subject matter claimed that can be carried out by one of ordinary skill in the pertinent art following the description contained in the reference....the determination of a practical utility when one is not obvious need **not** have been accomplished prior to the date of a reference unless the reference also teaches how to use the compound it describes. (*Id.* at 267, emphasis supplied).

Thus, *In re Moore* confirms the Stempel rule holding that in order to effectively remove a cited reference with a declaration under 37 C.F.R. § 1.131, an applicant need only show that portion of his or her claimed invention that appears in the cited reference. Moreover, *In re Moore* clearly stands for the proposition that when a cited reference discloses a claimed chemical compound either absent a utility or with a utility that is different from the one appearing in the claims at issue, a patent applicant can effectively swear back of that reference by simply showing prior possession of the claimed chemical compound. In other words, under this scenario, the patent applicant need not demonstrate that he or she had discovered a patentable utility for the claimed chemical compound prior to the effective date of the prior art reference.

This premise is also set forward in *In re Rainer*, 159 USPQ 334 (CCPA 1968), where the CCPA stated:

> "It is settled, of course, that an anticipatory disclosure, not a statutory bar, may be removed as a reference against a generic claim by a Rule 131 affidavit showing prior reduction to practice of as much of the claimed invention as the reference shows..." (Emphasis supplied).

Finally, the Examiner is respectfully directed to *In re Clarke*, 148 USPQ 665 (CCPA 1966), where the patent applicant (Clarke) filed a patent application claiming a genus of chemical compounds. The reference cited against the Clarke application was a publication showing one species falling within the scope of Clarke's generic claim. In response, Clarke submitted a declaration under 37 C.F.R. § 1.131 demonstrating that he had conceived of the claimed genus of

chemical compounds and had actually reduced to practice one species of the genus, however, that species was different from the one disclosed in the cited reference. In other words, Clarke was not able to show that he had actually reduced to practice the same chemical compound that was disclosed in the cited prior art reference. Thus, unlike the patent application in the *In re Stempel* case described above, Clarke did not show complete prior possession of the species disclosed in the cited prior art reference. Nevertheless, the CCPA held Clarke's 131 declaration effective if he showed that reduction to practice of the one species was sufficient to substantiate a claim to the whole genus which included the species disclosed in the reference. The CCPA indicated that such substantiation is provided if the reference species would have been obvious to one of ordinary skill in the art in light of what the applicant had completed prior to the invention. Specifically, the CCPA stated:

> "the [Stempel] rule for antedating references is **not** limited to fact situations where the inventor can show priority to the *identical* compound described in the reference...[a]n applicant should **not** be prevented from obtaining a patent to an invention where a compound described in a reference would have been obvious to one of ordinary skill in the art in view of what the affiant proves was completed with respect to the invention prior to the effective date of the reference....[W]here it can be concluded that facts, offered in a rule 131 affidavit in support of a general allegation of conception and reduction to practice of the invention, would persuade one of ordinary skill in the art to a reasonable certainty that the applicant possessed so much of the invention as to encompass the reference disclosure, then that showing should be accepted as establishing prima facie a case of inventorship prior to the reference.....Upon satisfying that test, **species of the reference falling within the claim may be antedated indirectly**." (Id. at 669-670, emphasis supplied).

Thus, *In re Clarke* makes clear that the Stempel rule described above extends to situations where the specific compound disclosed in the prior art reference is not identical to the compound actually reduced to practice by the patent applicant if (1) those compounds fall within the same genus and (2) the patent applicant demonstrates conception of that genus prior to the effective date of the prior art reference.

The Present Analysis

Applicants submit herewith a declaration under 37 C.F.R. § 1.131 signed by William I. Wood, Ph.D. (an inventor of the presently claimed subject matter) which serves to swear back of the herein cited references. More specifically, Dr. Wood provides facts demonstrating that the present Applicants had conceived of and reduced to practice the polypeptides of the present invention before the effective prior art dates of the herein cited references.

The herein cited references teach polypeptides which are either similar or identical to those claimed. None of the cited references, however, teach the specific utilities set forth for the presently claimed polypeptides (i.e., use as diagnostic targets to detect overexpression in human esophageal and/or lung cancer). Therefore, the only portion of the presently claimed invention that the herein cited references disclose are the actual polypeptide sequences disclosed. As such, in order to swear back of the herein cited references under the rules set forth by the CCPA in *In re Stempel*, 113 USPQ 77 (CCPA 1957), *In re Moore*, 170 USPQ 260 (CCPA 1971), *In re Rainer*, 159 USPQ 334 (CCPA 1968) and *In re Clarke*, 148 USPQ 665 (CCPA 1966) described above, Applicants need only demonstrate in a declaration under 37 C.F.R. § 1.131 (i) conception and reduction to practice of the polypeptides of the present claims prior to the effective prior art dates of the herein cited references. Applicants submit that the enclosed declaration under 37 C.F.R. § 1.131 by William I. Wood, Ph.D. does exactly that.

More specifically, the enclosed declaration under 37 C.F.R. § 1.131 by William I. Wood, Ph.D. demonstrates that the nucleic acid and polypeptide sequences of SEQ ID NO:59 and 60, respectively, were conceived of and actually reduced to practice prior to the effective dates of any of the herein cited references. Moreover, the enclosed declaration under 37 C.F.R. § 1.131 by William I. Wood, Ph.D. further demonstrates that a mature form of the polypeptide of present SEQ ID NO:60 as well a soluble extracellular domain form of the polypeptide of SEQ ID NO:60 were conceived of prior to the effective dates of any of the herein cited references. Finally, Dr. Wood also declares (and evidence of such is provided in the present application) that a cDNA corresponding

to SEQ ID NO:59 was deposited with the ATCC prior to the effective dates of the herein cited references. As such, under the rules set forth by the CCPA in *In re Stempel*, 113 USPQ 77 (CCPA 1957), *In re Moore*, 170 USPQ 260 (CCPA 1971), *In re Rainer*, 159 USPQ 334 (CCPA 1968) and *In re Clarke*, 148 USPQ 665 (CCPA 1966) described above, Applicants respectfully submit that the enclosed declaration under 37 C.F.R. § 1.131 by William I. Wood, Ph.D. serves to effectively remove the herein cited references as prior art that can be relied upon by the Examiner in support of a rejection under 35 U.S.C. § 102(e). Applicants, therefore, respectfully request reconsideration and withdrawal of the outstanding rejections under 35 U.S.C. § 102(e).

In light of the above amendments and remarks, Applicants believe that this application is now in condition for immediate allowance and respectfully request that the outstanding rejections be withdrawn and this case passed to issue.

The Examiner is invited to contact the undersigned at (650) 225-4461 if any issues may be resolved in that manner.

Respectfully submitted,

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By: _____

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